New insight into relationship between stress granules and angiogenin/RNase 5

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Angiogenin (ANG) is a 14-kDa extracellular protein originally identified in tumor cells conditioned media, ever since studied in several organs and involved in physiological and pathological processes [1]. Numerous evidences extended ANG biological activity from inducing angiogenesis to stimulating cell proliferation and more recently to promoting cell survival. Under stress conditions, ANG is accumulated in cytoplasmic compartments and modulates the production of tiRNAs, a novel class of small RNAs, that contribute to translational inhibition and recruitment of Stress Granules (SGs) [2]. To date, there are still limited experimental evidences relating to the role ANG in the epidermis, the outermost layer of human skin, continually exposed to external stressors. On the regard, our study is focused at clarifying ANG possible role in human keratinocytes (HaCaT cells) subjected to different stress stimuli.
Our results clearly indicate that in HaCaT cells endogenous ANG is localized both in the nucleus and in the cytoplasm, on the contrary, in stressed HaCaT cells the protein dramatically changes its localization moving largely towards transient cytoplasmic SGs. Further tests indicate that recombinant ANG is able to greatly limit the expression of heat shock proteins in stressed cells, to attenuate the number and size of SGs, to positively alter cell cycle and intriguingly also to induce an increase of expression of endogenous ANG.
As ANG is internalized and translocated to the nucleus after its binding to the cell surface receptor [3], additional experiments were carried out on a recombinant ANG variant in which nuclear translocation sequence between M30 to G34 was changed, in order to verify whether the inability to move to the nucleus actively alters cell response to stress conditions and/or its potential activity in promoting transcription. Collected results to date suggest that ANG could represent a promising protective strategy against skin damage skin damage.